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Review

The association between sleep duration and risk of abnormal lipid profile: A systematic review and meta-analysis

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ABSTRACT

Aims: The aim of this systematic review and meta-analysis is to assess the association between sleep duration and risk of abnormal lipid profile.
Main methods: PubMed, ISI Web of Science and Scopus were searched up to June 2016. Study-specific odds ratios (ORs) were pooled using a random-effects model. The protocol number of the study is PROSPERO 2016: CRD42016043919. A total of 13 articles including 83,037 participants were included in the meta-analysis.
Key findings: The pooled adjusted odds ratio (AOR) revealed that long sleep duration was significantly associated with the risk of high total cholesterol (TC) (AOR, 0.93; 95% CI, 0.87–0.99). However, neither short sleep nor long sleep duration was significantly associated with the risk of high triglycerides (TG), high Low-Density Lipoprotein-cholesterol (LDL-C) and low High-Density Lipoprotein-cholesterol (HDL-C). In the subgroup analysis based on different durations of sleep (≥8–9 h, ≥9–10 h, and ≥10 h) revealed, there was a dose-response relation observed with low HDL-c, high TC and high TG.
Significance: This review revealed that reliable evidence remained about the link between sleep duration and risk of abnormal lipid profile. Therefore, further large-scale well designed prospective studies should be warranted.

1. Introduction

Sleep is an important determinant of health and it is an essential necessity (Sivanesan and Bhatti, 2017). Its pattern in terms of quantity and quality are affected by a variety of factors including cultural, social, psychological, behavioral, pathophysiological, and environmental factors. Several studies have shown that sleep durations, both short and long have been associated with adverse health outcomes, including a higher risk for cardiovascular disease (Berentzen et al., 2014), diabetes mellitus (Chaput et al., 2009), hypertension (Fang et al., 2012), obesity (Adámková et al., 2009; Y. Wu, Zhai and Zhang, 2014), psychiatric disorders (Sharafi et al., 2020; Zitser et al., 2020) and total mortality (Kong et al., 2011).

An abnormal circulating lipid profile (hypertriglyceridemia, low serum High-Density Lipoprotein-cholesterol (HDL-C), elevated serum total cholesterol (TC), and high serum Low-Density Lipoprotein-cholesterol (LDL-C)) is a major indicator of atherosclerosis, and it is an established risk factor for cardiovascular disease (Bule et al., 2020; Nelson, 2013). A number of cross-sectional studies have found associations between sleep duration and the risk of lipid profile abnormalities such as hypercholesterolemia (Berentzen et al., 2014), hyperlipidemia (Grandner et al., 2014), high LDL-C and low HDL-C level (Kaneita et al., 2008; Zhan et al., 2014), however, other studies have not found any significant association (Lee and Park, 2014; Modesti et al., 2016).

Given several original studies have been published examining the effect of sleep duration on lipid profile, to our knowledge; this is the first meta-analysis that has been performed to investigate the association between sleep duration and risk of abnormal lipid profile. In this study, therefore, we performed a systematic review and meta-analysis to clarify the association between sleep duration and risk of abnormal lipid profile.

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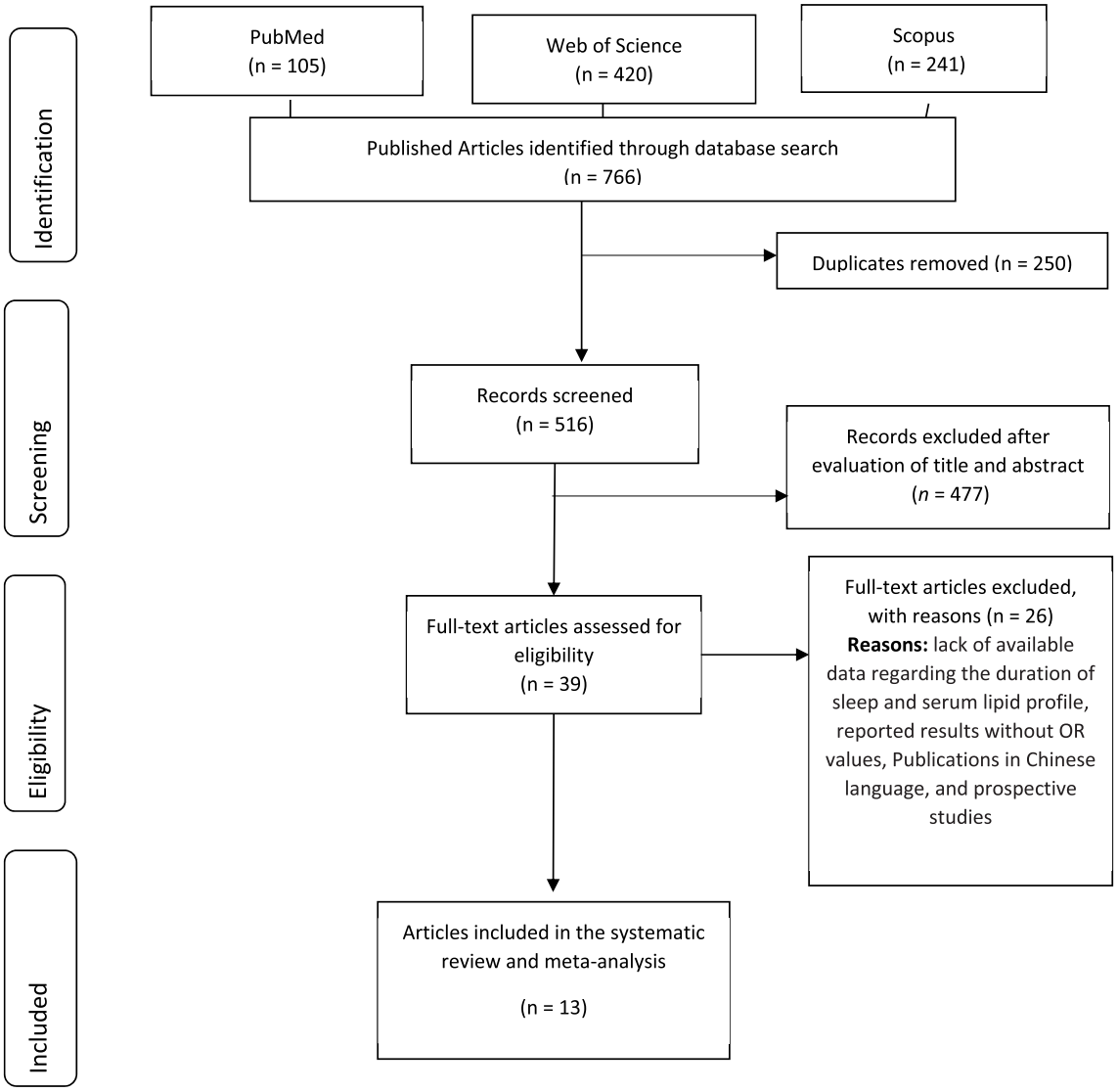
Identification
Screening
Eligibility
Included
PubMed
(n = 105)
Web of Science
(n = 420)
Scopus
(n = 241)
Published Articles identified through database search
(n = 766)
Duplicates removed (n = 250)
Records screened
(n = 516)
Records excluded after evaluation of title and abstract
(n = 477)
Full-text articles assessed for eligibility
(n = 39)
Full-text articles excluded, with reasons (n = 26)
Reasons: lack of available data regarding the duration of sleep and serum lipid profile, reported results without OR values, Publications in Chinese language, and prospective studies
Articles included in the systematic review and meta-analysis
(n = 13)

Fig. 1. PRISMA flow diagram for the systematic review and meta-analysis.

2. Materials and methods

2.1. Review design and search strategy

The protocol was registered in PROSPERO, the international database of registered systematic reviews (registration number: CRD42016043919). The PRISMA guideline was followed for performing and reporting the results of this meta-analysis (checklist reported in Appendix Table E1) (Moher et al., 2009). We developed a search strategy to identify observational studies that reported the association between duration of sleep and abnormal lipid profiles that were published until June 2016. Three databases including PubMed, ISI Web of Science and Scopus were searched using the terms "sleep duration", "dyslipidemia", "hyperlipidemia", "lipid profile", "cholesterol". Furthermore, we reviewed reference lists of original and review articles to search for more studies. Only those that were published as full-length articles were considered. English language restriction was applied to the search. Fig. 1 shows the study selection process.

PubMed was searched with the search strategy as follows: ((((Dyslipidemia [Title/Abstract] OR dyslipidemic [Title/Abstract] OR hyperlipidemic [Title/Abstract] OR hypolipidemic [Title/Abstract] OR hyperlipidemia [Title/Abstract] OR lipids [Title/Abstract] OR lipid profile [Title/Abstract] OR metabolic profile [Title/Abstract] OR cholesterol [Title/Abstract] OR triglyceride [Title/Abstract] OR TC [Title/Abstract] OR TG [Title/Abstract] OR LDL [Title/Abstract] OR LDL-C [Title/Abstract] OR LDL-cholesterol [Title/Abstract] OR HDL [Title/Abstract] OR HDL-C [Title/Abstract] OR HDL-cholesterol [Title/Abstract]) AND (sleep duration [Title/Abstract] OR sleep [Title/Abstract])) AND ("Humans"))

2.2. Eligibility criteria

Studies were included in this meta-analysis if they satisfied the following criteria: the study design was observational studies, the exposure of interest was sleep duration (short or long), the outcome was lipid profile abnormalities (high TC, high TG, high LDL or/and low HDL) and the investigators reported adjusted odds ratios (AORs) with 95% CIs for at least two quantitative categories of short sleep or long sleep duration for each serum lipid profile. We excluded animal studies, clinical trials, reviews, commentaries, letters, and studies that examined other associations other than sleep duration and lipid profile. If study populations were reported more than once, we used the result with the most updated data. The eligibility of each abstract or full-text article was assessed independently in a standardized manner by two investigators (A.A. and S.R.).

2.3. Data extraction

Two independent reviewers serially abstracted data from selected articles using an electronic abstraction database created in Microsoft Excel (Microsoft Corporation, Seattle, WA). Information abstracted included first author's name, year of publication, country of data collection, study design, number of participants and sample characteristics (age and sex), method used to measure sleep duration, reference category of sleep, category for "short" and "long" sleep, covariates adjusted in the multivariable analysis, and AORs with 95% CIs (adjusted by the most confounders in the original studies) for all categories of sleep duration as compared with the reference sleep duration. Any disagreements that arose between the reviewers about review selection were resolved by discussion and consensus.

2.4. Quality of assessment

The quality and strength of the included articles were assessed by the modified Newcastle–Ottawa Scale for nonrandomized studies (Wells et al., 2014). The following parameters were assessed: sampling strategy, inclusion/exclusion criteria, sample size, cut-offs and reference for the assessment of sleep duration, criteria to identify lipid profiles and covariates included in statistical models. The final scoring system comprised 11 criteria of rating different quality elements for each eligible paper out of 12 scores (Supplementary Table 1). The authors recommended scale weights for each element of the scoring system, as proposed in other meta-analyses. Studies were classified into three groups based on their quality score: 'A' if they managed to obtain 9–12 points, 'B' when 5–8 points were collected and 'C' when they scored less than 5 points. Studies of high quality, with the less estimated risk of bias, were allocated to class 'A' and were subsequently used in the sensitivity analyses.

2.5. Statistical analysis

The strength of association between sleep duration (short or long) and risk of lipid profile abnormality (high TC, high TG, high LDL and low HDL) was estimated by calculating pooled Adjusted Odds Ratio (AOR) and 95% CI. A random-effects model (DerSimonian-Laird method) (DerSimonian and Laird, 1986) was used to account for variance between the studies as well as within the studies. This was decided, a priori, as the study population to be analyzed in our meta-analysis was heterogeneous. Additionally, the heterogeneity was separately estimated using a $\chi 2$ test, Q statistics with corresponding p values, and I^2 statistics. In analyses where $p \leq 0.1$ or $I^2 \geq 50\%$ was observed, we explored possible sources of heterogeneity by subgroup analyses based on different durations of sleep (per hour), number of participants (≥ 5000 or < 5000), Country, age and sex of participants. The effect of aberrant studies was examined via sensitivity analyses after the exclusion of studies with low and poor quality, as classified by the quality scoring system (B and C class studies). Moreover, an influence analysis after excluding one study at a time was performed to assess the stability of the results, an individual study was suspected of excessive influence if the point estimate of its omitted analysis lay outside the 95% CI of the combined analysis. Publication bias was assessed by Begg's test and Egger's test ($p < 0.05$ was considered statistically significant) (Egger M, 2008). Statistical analysis was conducted using STATA version 12 (StataCorp LP, College Station, Texas, USA).

3. Results

3.1. Search results

A flow chart for exclusion/inclusion of individual articles (or studies) was presented in Fig. 1. The literature search identified a total of 766 (PubMed- 105, ISI Web of Sciences- 420 and Scopus- 241) potentially relevant papers. We excluded 730 articles, including 250 duplicated articles: 480 papers were excluded after reading the title and abstract because of obvious irrelevance. Then 36 full-text articles were retrieved and carefully evaluated, and 19 of these studies were excluded because of a lack of available data regarding the duration of sleep and serum lipid profile. The remaining 17 studies were carefully analyzed, and 4 studies were excluded because of lack of suitable sleep time categorization, they provided data only on the prospective association between sleep duration and lipid profile, and reported results were without OR values. Results from seven articles (Azadbakht et al., 2013; Berentzen et al., 2014; Kaneita et al., 2008; Kong et al., 2011; Sabanayagam and Shankar, 2012; J. Wu et al., 2015; Zhan et al., 2014) were presented according to sex, and these were considered as separate studies in the data analysis. Therefore, 13 articles including 19 studies were ultimately included in the meta-analysis (Berentzen et al., 2014; Bjorvatn et al., 2007; Chang et al., 2015; Grandner et al., 2014; Kaneita et al., 2008; Kong et al., 2011; Lee and Park, 2014; Lin et al., 2016; Modesti et al., 2016; Sabanayagam and Shankar, 2012; J. Wu et al., 2015; Zhan et al., 2014).

3.2. Characteristics of the studies

The meta-analysis included 83,037 participants from 9 different countries (3 studies from China, 2 from the USA, 2 from Taiwan, and 1 each from Japan, Korea, Italy, Norway, Iran, and the Netherlands). The participants of all the included studies were healthy individuals. Twelve articles recruited both men and women, while one recruited only men. Of the twelve articles that included both men and women, seven reported outcomes separately for men and women. The age of the participants ranged from 10 to 98 years. All of the studies reported ORs adjusted for different confounders. The most commonly adjusted confounders included, age, sex, BMI, smoking, and physical activity (Table 1).

Self-reported sleep duration was supplied in all included studies. Among the included studies, three studies defined short sleep as a duration of ≤ 5 h (Azadbakht et al., 2013; Lee and Park, 2014; Sabanayagam and Shankar, 2012), seven studies as < 6 or ≤ 6 h (Bjorvatn et al., 2007; Chang et al., 2015; Grandner et al., 2014; Kaneita et al., 2008; Lin et al., 2016; Modesti et al., 2016; Zhan et al., 2014), two studies as < 7 h (Kong et al., 2011; J. Wu et al., 2015), and the remaining one article defined it as < 7.5 h (Berentzen et al., 2014). Long sleep was defined as ≥ 8 h (Azadbakht et al., 2013; Berentzen et al., 2014; Chang et al., 2015; Kaneita et al., 2008; Kong et al., 2011; Sabanayagam and Shankar, 2012; J. Wu et al., 2015), ≥ 9 h (Bjorvatn et al., 2007; Grandner et al., 2014) and ≥ 10 h (Modesti et al., 2016; Zhan et al., 2014),[(Berentzen et al., 2014)] (Table 1). For the present analysis, short and long sleep was defined as a duration of < 7 h, and ≥ 8 h, respectively.

The main outcomes studied were abnormal serum lipids in five studies, metabolic syndrome and its components in four studies, and cardio-metabolic risk including hypertension, hyperlipidemia, DM, and obesity in four studies. Eleven studies collected fasting blood samples, but two studies collected non-fasting blood samples. The serum TG, HDL-C, LDL, and TC levels were measured using standard procedure in eleven studies; however, Yoshitaka K. et al., 2008 and Kong AP et al., 2011 (Kong et al., 2011) used Friedewald's method to determine the level of LDL-C. Hypercholesterolemia was defined as fasting TC $\geq$ 240 mg/dl (Grandner et al., 2014; Kong et al., 2011; Lin et al., 2016; Modesti et al., 2016), hypertriglyceridemia was defined as fasting TG $\geq$ 150 mg/dl (1.7 mol/l) (Chang et al., 2015; Kaneita et al., 2008; Kong et al., 2011; J. Wu et al., 2015), or fasting TG $\geq$ 110 mg/dL (Lee and Park, 2014), or TG $>$ 200 mg/dl (Bjorvatn et al., 2007; Modesti et al., 2016), low HDL was defined as fasting HDL cholesterol $<$ 40 mg/dL (1.04 mmol/L) for men or $<$ 50 mg/dL (1.29 mmol/L) for women; and LDL cholesterol level $\geq$140 mg/dL was considered to be high

Table 1
Summary of main characteristics of the selected studies.

Author	Year of Publication	Country	Study pop.	Pop. type	Sex	Age (Year)	Method used to measure sleep duration	Sleep Category	Evaluated Parameter	Covariates Adjusted	Quality score
Azadbakht L	2013	Iran	5528	Healthy Ind.	M&F	10–18	Sleep-reported Questionnaires	Ref: < 5 h Short:5–8 h Long: > 8 h	TC, TG, LDL	Age, SES, parents' educations, family history of chronic disease, sedentary lifestyle, and BMI	9
B J Ø R N B J O R V A T N	2006	Norway	8860	Healthy Ind.	M&F	40–45	Sleep-reported questionnaires	Ref:7–8 h Short: < 6 h Long: ≥9 h	TC, TG, HDL	Gender, smoking, BMI	11.5
Bertentzen NE.	2013	Netherlands	1481	Healthy Ind.	M&F	11–12	Sleep-reported Questionnaires	Ref:9.5–11 h Short:7.5–9.5 h Long: 11–12.5 h	TC, HDL	Height, mother's education, puberty development and screen time	7
Charumathi S.	2008	USA	16,652	Healthy Ind.	M&F	≥18	Sleep-reported questionnaires	Ref: 7 h Short: ≤5 h Long: ≥8 h	TC	Age, race/ethnicity, education, smoking, alcohol intake, physical inactivity, and psychological distress.	8.5
Chia-Ling Lin	2015	Taiwan	1533	Healthy Ind.	M&F	19–64	Sleep-reported questionnaires	Ref: > 6 h Short: < 6 h Long: NA	TC	Age, sex, fasting plasma glucose, body mass index, waist circumstance, hypertension and diabetes.	8.5
J.A. Lee	2013	Korea	1187	Healthy Ind.	M&F	12–18	Sleep-reported questionnaires	Ref:8–9 h Short:≤5 h Long:≥10 h	TG, HDL	Age, sex, household income, caloric intake, and physical activity.	8.5
JEN-HUNG CHANG	2015	Taiwan	796	Healthy Ind.	M	37.36 ± 7.73	Sleep-reported questionnaires	Ref:7–8 h Short: < 6 h Long: ≥8 h	TG, HDL	Age, LDL, smoking status, alcohol drinking habit, physical habitual exercise, snoring and type of shift work	12
Jing Wu	2015	China	25,184	Healthy Ind.	M&F	mean 63.6	Sleep-reported questionnaires	Ref:7–8 h Short: < 7 h Long: ≥8 h	TG, HDL	age, marriage, education, smoking status, drinking status, physical activity, coronary heart disease, myocardial infarction, stroke	9
Kong AP.	2010	China	2053	Healthy Ind.	M&F	< 18	Sleep-reported Questionnaires	Ref: < 6.5 h Long: > 8 h	TC, TG, HDL, LDL	Age, gender, BMI, and pubertal stage	11
Michael A. Grandner	2013	USA	5649	Healthy Ind.	M&F	≥18	Sleep-reported questionnaires	Ref: 7–8 h Short: ≤5 h Long: ≥9 h	TC	Age, sex, race/ethnicity, acculturation, education, insurance, home ownership, food security, smoking, and caffeine use.	7
Pietro A. Modesti	2016	Italy	1608	Healthy Ind.	M&F	16–59	Sleep-reported questionnaires	Ref: ≤5 h Short: ≤6 h Long: NA	TG	Age, sex, snoring frequency, and BMI	11
Yiqiang Zhan	2014	China	8511	Healthy Ind.	M&F	18–98	Sleep-reported questionnaires	Ref: 8 h Short: ≤6 h Long: ≥10 h	TC, TG, LDL, HDL	sleep duration, age, education, occupation, current smoking, current drinking, physical activity, body mass index, hypertension, and diabetes	9
Yoshitaka Kaneita	2008	Japan	3995	Healthy Ind.	M&F	≥20	Sleep-reported questionnaires	Ref:6–7 h Short: < 6 h Long: ≥8 h	TG, LDL, HDL	Age, blood pressure, body mass index, fasting plasma glucose level, smoking habit, alcohol consumption, dining habits, psychological stress, and using anti-lesterol medicine	8

M: Male, F: Female, NA: Not Applicable, TC: Total Cholesterol, TG: Triglyceride, LDL: Low Density Triglyceride, HDL: High Density Triglyceride, h: hour, Ref: Referent, Pop: Population, Healthy Ind. Healthy Individual, SES Socioeconomic status.

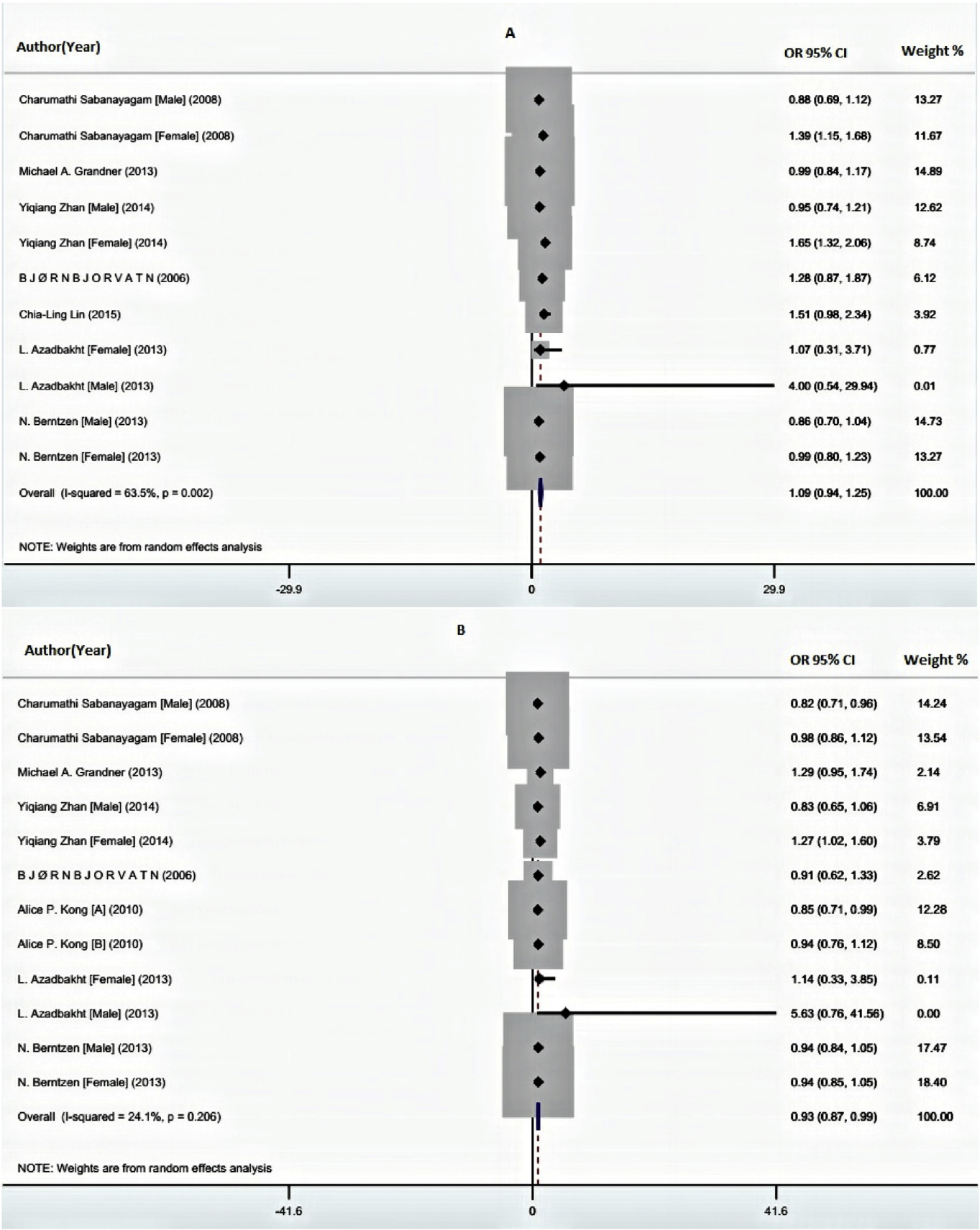
A
Author(Year)
OR 95% CI
Weight %
Charumathi Sabanayagam [Male] (2008) 0.88 (0.69, 1.12) 13.27
Charumathi Sabanayagam [Female] (2008) 1.39 (1.15, 1.68) 11.67
Michael A. Grandner (2013) 0.99 (0.84, 1.17) 14.89
Yiqiang Zhan [Male] (2014) 0.95 (0.74, 1.21) 12.62
Yiqiang Zhan [Female] (2014) 1.65 (1.32, 2.06) 8.74
B J Ø R N B J O R V A T N (2006) 1.28 (0.87, 1.87) 6.12
Chia-Ling Lin (2015) 1.51 (0.98, 2.34) 3.92
L. Azadbakht [Female] (2013) 1.07 (0.31, 3.71) 0.77
L. Azadbakht [Male] (2013) 4.00 (0.54, 29.94) 0.01
N. Berntzen [Male] (2013) 0.86 (0.70, 1.04) 14.73
N. Berntzen [Female] (2013) 0.99 (0.80, 1.23) 13.27
Overall (I-squared = 63.5%, p = 0.002) 1.09 (0.94, 1.25) 100.00
NOTE: Weights are from random effects analysis
-29.9
0
29.9
B
Author(Year)
OR 95% CI
Weight %
Charumathi Sabanayagam [Male] (2008) 0.82 (0.71, 0.96) 14.24
Charumathi Sabanayagam [Female] (2008) 0.98 (0.86, 1.12) 13.54
Michael A. Grandner (2013) 1.29 (0.95, 1.74) 2.14
Yiqiang Zhan [Male] (2014) 0.83 (0.65, 1.06) 6.91
Yiqiang Zhan [Female] (2014) 1.27 (1.02, 1.60) 3.79
B J Ø R N B J O R V A T N (2006) 0.91 (0.62, 1.33) 2.62
Alice P. Kong [A] (2010) 0.85 (0.71, 0.99) 12.28
Alice P. Kong [B] (2010) 0.94 (0.76, 1.12) 8.50
L. Azadbakht [Female] (2013) 1.14 (0.33, 3.85) 0.11
L. Azadbakht [Male] (2013) 5.63 (0.76, 41.56) 0.00
N. Berntzen [Male] (2013) 0.94 (0.84, 1.05) 17.47
N. Berntzen [Female] (2013) 0.94 (0.85, 1.05) 18.40
Overall (I-squared = 24.1%, p = 0.206) 0.93 (0.87, 0.99) 100.00
NOTE: Weights are from random effects analysis
-41.6
0
41.6

Fig. 2. Meta-analysis of the association between short sleep (A) and long sleep (B) with high TC.

(Chang et al., 2015; Kaneita et al., 2008; Kong et al., 2011; Lee and Park, 2014; J. Wu et al., 2015). In three studies, hypercholesterolemia was ascertained by medical records or self-reports (Berentzen et al., 2014; Grandner et al., 2014; Sabanayagam and Shankar, 2012). In two studies, lipid abnormality was ascertained by the current use of medication treatment for reduced or elevated serum lipid (Chang et al., 2015; Grandner et al., 2014).

3.3. Quantitative synthesis

3.3.1. Association between sleep duration and high TC

Seven studies involving 48,264 participants were included in the short sleep duration meta-analysis. The overall result indicated that short sleep duration was not significantly associated with the risk of high TC (OR, 1.09; 95% CI, 0.94–1.25; I^2 = 63.5%, p = 0.002) (Fig. 2). Four articles (Azadbakht et al., 2013; Berentzen et al., 2014; Kong et al., 2011; Zhan et al., 2014) reported separate results for men and women, thus, pooled measures were calculated separately by gender for these studies. Also, there was no statistically significant association was observed, however, the between-study heterogeneity was reduced. Similarly, in another subgroup analysis by age, the number of participants, and Country, a non-significant association was found (Supplemental Table 2).

Twelve studies involving 48,734 participants were included in the long sleep duration and high TC meta-analysis. The overall result indicated that long sleep duration was significantly associated with the risk of high TC (OR, 0.93; 95% CI, 0.87–0.99; I^2 = 24.1%, p = 0.21) (Fig. 2). In the subgroup analysis by age, gender, number of participants, and Country, a non-significant association was also found. Subgroup analyses to explore heterogeneity showed that the heterogeneity was explained by the participant's gender of included studies (Supplemental Table 2).

Sub-group analyses based on different durations of short sleep revealed that there was no dose response relation with high TC relationship. Duration of sleep ≤5 h, 5–6 h, and 6–7 h had pooled ORs of 1.25 ([95% CIs: 0.96 to 1.53; I^2 = 66.4%, p = 0.018), 0.97 ([95% CIs: 0.85 to 1.09; I^2 = 0.0%, p = 0.93), 1.06 ([95% CI: 0.89 to 1.23; I^2 = 77.5%, p = 0.001), respectively. Pooled estimates of the ORs for long sleep duration groups (≥8–9 h) were revealed dose response relation was observed with high TC relationship 0.91 ([95% CIs: 0.85 to 0.97]; I^2 = 0.0%, p = 0.45), however no dose response relations were observed for long sleeps duration (≥9–10 h, and ≥10 h) 1.01 ([95% CIs: 0.85 to 1.16]; I^2 = 56.0%, p = 0.04), and 0.96 ([95% CIs: 0.85 to 1.0; I^2 = 50.4%, p = 0.11), respectively (Supplemental Table 3).

3.3.2. Association between sleep duration and high TG

A meta-analysis of twelve studies involving 55,669 participants indicated that short sleep duration was not significantly associated with the risk of high TG (OR, 1.06; 95% CI, 0.90–1.22; I^2 = 55.1%, p = 0.01) (Table 2). In the subgroup analysis by age, gender, number of participants, and Country, a non-significant association was also found (Supplemental Table 2).

Twelve studies involving 55,669 participants were included in the long sleep duration and high TG meta-analysis. The overall result indicated that long sleep duration was not significantly associated with the risk of high TG (OR, 1.07; 95% CI, 0.97–1.16; I^2 = 47.8%, p = 0.02) (Table 2). In the subgroup analysis by age, gender, number of participants, and Country, a non-significant association was found. Subgroup analyses to explore heterogeneity showed that the heterogeneity was explained by the sample size of the included studies (Supplemental Table 2).

Sub-group analyses based on different durations of short sleep revealed that there was no dose response relation with high TG relationship. Duration of sleep ≤5 h, 5–6 h, and 6–7 h had pooled ORs of 1.08 ([95% CIs: 0.48 to 1.68; I^2 = 78.4%, p = 0.003), 1.03 ([95% CIs: 0.82 to 1.24; I^2 = 43.6%, p = 0.08), and 1.00 ([95% CI: 0.85 to 1.16; I^2 = 55.2%, p = 0.03), respectively. Pooled estimates of the ORs for long sleep duration groups (≥8–9 h, and ≥10 h) were revealed dose response relation with high TG relationship 1.06 ([95% CIs: 1.01 to 1.11; I^2 = 0.0%, p = 0.45), and 1.26 ([95% CIs: 1.05 to 1.48; I^2 = 59.6%, p = 0.04), respectively (Supplemental Table 3).

3.3.3. Association between sleep duration and high LDL

Six studies involving 18,034 participants were included in the short sleep duration and high LDL meta-analysis. The overall result indicated that short sleep duration was not significantly associated with the risk of high LDL (OR, 1.06; 95% CI, 0.80–1.32; I^2 = 44.1%, p = 0.11) (Table 2). In the subgroup analysis by age, gender, number of participants, and Country, a non-significant association was also found. Subgroup analyses to explore heterogeneity showed that the heterogeneity was explained by the participant's gender of included studies (Supplemental Table 2).

Eight studies involving 20,087 participants were included in the long sleep duration and high LDL meta-analysis. The overall result indicated that long sleep duration was not significantly associated with the risk of high LDL (OR, 0.84; 95% CI, 0.68–1.00; I^2 = 59.6%, p = 0.01) (Table 2). In the subgroup, analysis by age, gender, number of participants, and Country, a non-significant association was found, whereas, the between-study heterogeneity declined (Supplemental Table 2).

Sub-group analyses based on different durations of short sleep revealed no dose response relationship with high LDL. Duration of sleep ≤5 h, 5–6 h, and 6–7 h had pooled ORs of 0.95 ([95% CIs: 0.38 to 1.52; I^2 = 45.2%, p = 0.18), 0.89 ([95% CIs: 0.70 to 1.08; I^2 = 0.0%, p = 0.99), 1.33 ([95% CI: 0.64 to 2.03; I^2 = 79.4%, p = 0.03), respectively. Pooled estimates of the ORs for long sleep duration groups (≥8–9 h, ≥9–10 h, and ≥10 h) were revealed no dose response relation with high LDL relationship 0.83 ([95% CIs: 0.63 to 1.03]; I^2 = 65.8%, p = 0.01), 1.00 ([95% CIs: 0.75 to 1.25]; I^2 = 0.0%, p = 0.75), and 0.87 ([95% CIs: 0.48 to 1.26]; I^2 = 63.0%, p = 0.10), respectively (Supplemental Table 3).

3.3.4. Association between sleep duration and low HDL

Eleven studies involving 50,014 participants were included in the short sleep duration and low HDL meta-analysis. The overall result indicated that short sleep duration was not significantly associated with the low level of HDL (OR, 1.03; 95% CI, 0.97–1.09; I^2 = 0.0%, p = 0.59) (Table 2). In the subgroup analysis by age, gender, number of participants, and Country, a non-significant association was also found (Supplemental Table 2).

Thirteen studies involving 52,067 participants were included in the long sleep duration and low HDL meta-analysis. The overall result

Table 2
Random-effect meta-analysis of the association between short sleep and long sleep with high TG, high LDL and low HDL.

Pooled Analysis	Short sleep duration		Long Sleep duration	
Parameters	Pooled OR (95 %CI)	I^2, *p*	Pooled OR (95 %CI)	I^2, *p*
High triglycerides	1.06 (0.90–1.22)	55.1%, 0.01	1.07 (0.97–1.16)	47.8%, 0.02
High LDL	1.068 (0.80–1.32)	44.1%, 0.11	0.84 (0.68–1.00)	59.6%, 0.01
Low HDL	1.03 (0.97–1.09)	0.0%, 0.59	1.00 (0.95–1.04)	34.5%, 0.11

indicated that long sleep duration was not significantly associated with the risk of low HDL (OR, 1.00; 95% CI, 0.95–1.04; I^2 = 34.5%, p = 0.11) (Table 2). In the subgroup analysis by age, gender, number of participants, and Country, a non-significant association was found (Supplemental Table 2).

Sub-group analyses based on different durations of short sleep did not reveal any dose response relationship with low HDL. Duration of sleep ≤5 h, 5–6 h, and 6–7 h had pooled ORs of 1.25 ([95% CIs: 0.88 to 1.63; I^2 = 0.0%, p = 0.62), 0.92 ([95% CIs: 0.70 to 1.14; I^2 = 14.0%, p = 0.32), and 1.00 ([95% CI: 0.90 to 1.09; I^2 = 0.0%, p = 0.84), respectively. Pooled estimates of the ORs for long sleep duration groups (≥9–10 h, and ≥10 h) were revealed dose response relation with low HDL-c relationship 1.14 ([95% CIs: 1.04 to 1.24; I^2 = 0.0%, p = 0.88), and 1.07 ([95% CIs: 1.00 to 1.15]; I^2 = 54.6%, p = 0.04), respectively (Supplemental Table 3).

3.4. Sensitivity analysis and influence analysis

Sensitivity analysis was performed to examine the influence of low quality and high-bias-risk studies on the overall estimate. According to the quality score (Table 2), only studies of higher quality (n = 7, 53.8%) were included in the sensitivity analysis. The sensitivity analyses resulted, both short and long duration of sleep were not significantly associated with the risk of high TC, high TG, high LDL-c, and low level of HDL-c (Table 3).

After excluding one study at a time (by Bjorvatn B. et al. for high TC, high TG and low HDL; and by Kaneita Y. et al. for high LDL; studies with the largest influence), the influence analysis confirmed, the non-significant association remained between both short sleep duration and long sleep duration, and lipid abnormality [high TG, high TC, high LDL-c and low HDL-c] (Table 3).

3.5. Publication bias

Begg and Egger regression tests provided no evidence of substantial publication bias for the analysis between both short sleep duration and long sleep duration, and lipid abnormality (P > 0.05 for all tests) (data not shown).

4. Discussion

The present systematic review and meta-analysis aimed to summarize the findings of population-based cross-sectional studies examining the association between sleep duration and risk of abnormal lipid profile. The findings from the quantitative analyses showed that only long sleep duration was associated with the risk of high TC. On the other hand, neither short nor long sleep duration was significantly associated with the risk of serum lipid abnormality (high TG, high LDL-c and low HDL-c). The review revealed that reliable evidence still remained about the link between sleep duration and risk of abnormal lipid profile.

However, in the subgroup analysis based on different durations of sleep, we found long sleep durations (≥9–10 h and ≥10 h) were accompanied by some higher risk of low HDL; and long sleep duration (≥8–9 h) was significantly associated with increased risk of high TC. Similarly, the sleep duration group (≥8–9 h and ≥10 h) was significantly associated with an increased risk of high TG. This indicates that excessively long period of sleep to be associated with a higher risk factor for high TC, high TG and low HDL. On the other hand, the subgroup analysis by age, gender, number of participants, and Country showed that both short and long sleep durations were not significantly associated with abnormal lipid profiles.

In this study, we found heterogeneity among studies; therefore, subgroup analysis was performed to find the possible source of heterogeneity based on different durations of sleep, number of participants, Country of the study, age, and gender of participants. The subgroup analysis based on different durations of sleep (≥8–9 h, ≥9–10 h, and ≥10 h) revealed, there was dose-response relation observed with low HDL-c and high TG, whereas the I^2 declined in all, indicating that duration of sleep, age, gender, and Country of study contributes to the high level of heterogeneity.

Previous published epidemiological studies have been reported inconsistent findings and still, the relationship between sleep duration and abnormal lipid profile has remained debatable (Arora et al., 2011; Hall et al., 2008; Kaneita et al., 2008; Van den Berg et al., 2008). In addition, there is accumulating evidence that shorter sleep duration is becoming another pervasive problem in today's society (Hasler et al., 2004). Because of the cross-sectional nature of these data, it cannot be used to draw conclusions on the cause-and-effect relationship. The possible reason could be partly due to a lack of consensus about the exact cut point to define short or long sleep duration and different categories of sleep duration was used across studies. For example, the definitions of short sleep duration ranged from ≤5 to < 7 h per day, and the definitions of long sleep duration ranged from ≥8 to ≥10 h per day, and different reference groups ranging from ≤5 to < 9 h per day. Therefore, these differences could yield different results. Similar to our results, a recent systematic review presented inconclusive evidence for the association between hours of sleep and lipid profile (Abreu et al., 2015).

In the present study, the subgroup analysis by gender of participants revealed that both short and long sleep duration was not associated with the risk of high TC and high TG in both sexes. These findings are

Table 3
Sensitivity and influence analysis.

Sensitivity Analysis	Short sleep duration		Long Sleep duration	
Parameters	Pooled OR (95 %CI)	I^2, *p*	Pooled OR (95 %CI)	I^2, *p*
High total cholesterol	1.26 (0.86–1.67)	60.7%, 0.04	0.93 (0.81–1.04)	20.9%, 0.27
High triglycerides	1.09 (0.89–1.29)	43.6%, 0.09	1.05 (0.95–1.16)	56.8%, 0.01
Low HDL	0.98 (0.87–1.09)	0.0%, 0.52	1.00 (0.93–1.07)	39.4%, 0.12
High LDL	1.30 (0.82–1.78)	39.0%, 0.17	0.91 (0.83–1.00)	0.0%, 0.43
Influence Analysis/Excluded Study				
High total cholesterol				
B J Ø R N B J O R V A T N et al., 2006	1.08 (0.92, 1.24)	66.8%, 0.01	0.93 (0.87, 0.99)	31.0%, 0.15
High triglycerides				
B J Ø R N B J O R V A T N et al., 2006	1.07 (0.88, 1.26)	59.0%, 0.01	1.07 (0.97, 1.17)	51.7%, 0.02
Low HDL				
B J Ø R N B J O R V A T N et al., 2006	1.05 (0.98, 1.11)	0.0%, 0.83	1.00 (0.95, 1.04)	37.4%, 0.09
High LDL				
Y. Kaneita et al., (2008)	1.30 (0.82, 1.78)	39.0%, 0.18	0.91 (0.83, 1.00)	0.0%, 0.44

inconsistent with previous results presenting sleep deprivation to increase TC and TG levels. The short duration of sleep could increase the risk for high TC and TG by increasing appetite and dietary consumption of saturated fats and by increasing stress and resultant catecholamine-induced lipolysis (Spiegel et al., 2004). Additionally, these associations could be partly explained by sex differences in the lipid parameters. Women have higher TC and TG than men (Hickman et al., 1998). Women have higher HDL levels (TELL, MITTELMARK, & VELLAR, 1985) and lower circulating cortisol than men (Van Cauter, Leproult and Kupfer, 1996).

The potential mechanisms other than lipid profiles that may confer increased CVD risk to short sleepers include sympathetic nervous activation, which is likely to be a mediator for the development of obesity through effects on the secretion of peripheral hormones that regulate appetite and energy expenditure (Knutson KL. & Van Cauter E, 2008). Increased sympathetic activity is also a mediator for hypertension, glucose intolerance and inflammation (Arora et al., 2011; Nagai et al., 2010). Short sleep also affects the neuroendocrine hormone axis (e.g., growth hormone suppression), which promotes obesity and metabolic syndrome (AlDabal and BaHammam, 2011).

Our meta-analysis has several strengths. We analyzed by including a large number of participants (83,037 participants) in 13 different studies from nine different countries. Therefore, the results are generalizable for the most part, as the study participants are from different ethnic background with different age range. We carried out sensitivity analyses and influential analysis for the main analysis; we were able to identify a significant association between short duration of sleep with some lipid profiles. We also extensively searched possible sources of heterogeneity separately for each analysis. Heterogeneity was mostly explained by duration of sleep, age, gender, number of participants, and Country of the study conducted. Furthermore, the high quality of most of the included studies was the strength of the present review.

However, our study is subject to several limitations. First, in the review as we used cross-sectional studies, it could not be determined cause and effect relation, even for factors between which an association was indicated. However, longitudinal study such as a cohort study is warranted, and such study should be included in the future works. Second, all the included studies measured the sleep duration using a self-reported sleep duration questionnaire, and this could have a bias due to subjectivity. Though, self-reported sleep duration assessment is well associated with values obtained with an actigraphic monitoring (Cespedes et al., 2016). Third, there was significant heterogeneity in the samples of the retrieved studies. In order to explore the source of heterogeneity, subgroup analyses have been performed, and sensitivity analyses were done. Thus, random effect models were used for meta-analysis, considering the likelihood of significant heterogeneity amongst studies.

In conclusion, the present meta-analysis suggested that in the pooled analysis only long sleep duration was associated with the risk of high TC. However, neither short nor long sleep duration was significantly associated with the risk of serum lipid abnormality (high TG, high LDL-c and low HDL-c). In the subgroup analysis by the duration of sleep, there was a dose-response association found between sleep duration and abnormal lipid profile (i.e. high TC, high TG and low HDL-c). Therefore, further large-scale well designed prospective studies should be conducted on this issue to explain and demonstrate the nature of this association and the involved biological mechanisms. Since abnormal lipid profile has a strong association with cardiovascular risks, it is critical to identify and modify factors that are related to abnormal lipid profile (Nelson, 2013).

Disclaimers

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Author contributions

Conception and design of the research, Analysis and interpretation of the data and Critical revision of the manuscript for intellectual content: Ahmed Abdulahi Abdurahman, Shahabeddin Rezaei, Dr. Sakineh Shab-Bidar and Dr. Kurosh Djafarian; Acquisition of data: Mohammed Bule, Ahmed Abdulahi Abdurahman and Shahabeddin Rezaei; Writing of the manuscript: Ahmed Abdulahi Abdurahman.

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CRediT authorship contribution statement

Ahmed A. Abdurahman: Data curation, Writing - original draft, Writing - review & editing. **Mohammed Bule:** Data curation, Writing - original draft, Writing - review & editing. **Sakineh Shab-Bidar:** Conceptualization, Methodology, Software. **Shahabeddin Rezaei:** Formal analysis, Writing - original draft, Writing - review & editing. **Kourosh Djafarian:** Conceptualization, Methodology, Software.

Declaration of competing interest

Authors declare no conflict of interest.

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Appendix A. Supplementary data

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